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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	25

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/826,361	Mosselman et al.
Examiner	**Art Unit**
Michael Pak	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *May 22, 2001* .

2a) [X] This action is **FINAL.** 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-12, 14-18, and 20-26* is/are pending in the application.

4a) Of the above, claim(s) *9-11, 14, and 18* is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1-3, 6-8, 12, 15-17, and 20-26* is/are rejected.

7) [X] Claim(s) *4 and 5* is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [ ] Notice of References Cited (PTO-892)

16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) [ ] Interview Summary (PTO-413) Paper No(s). _____

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other:

DETAILED ACTION

Response to Amendment

1. Amendments filed 22 May 2001 (Paper No. 24) and filed 22 March 2001 (Paper No. 23) have been entered.

2. Applicant's arguments filed 22 May 2001 (Paper No. 24) and filed 22 March 2001 (Paper No. 23) have been fully considered but they are not found persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This application contains claims 9-11, 14 and 18 drawn to an invention non-elected with traverse in Paper No. 14. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) MPEP § 821.01.

Claim Rejections - 35 USC § 112

5. Claims 1-3, 6-8, 12, 15-17, and 20-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA encoding a protein comprising SEQ ID NO: 5, 6, 21, or 25, does not reasonably provide enablement for,

A) an isolated DNA encoding a protein having an N-terminal domain, a DNA binding domain, and a ligand binding domain, wherein the amino acid sequence of said DNA-binding domain of said protein exhibits at least 80% or 90% homology with the amino acid sequence of SEQ ID NO:3 and the amino acid sequence of said ligand binding domain of said protein exhibits at least 70% or 75% homology with the amino acid sequence of SEQ ID NO:4 wherein the DNA binding domain targets the receptor protein to a selected hormone responsive element of a target gene and said ligand-binding domain recognizes and binds to an estrogen, thereby modulating expression of said target gene;

B) a recombinant expression vector comprising the isolated DNA of A) above;

C) a cell transfected with the DNA of A) above or the recombinant expression vector of B) above;

D) a DNA of claim 12 encoding a chimeric protein;

E) an isolated DNA encoding a protein having an N-terminal domain, a DNA binding domain, and a ligand binding domain, wherein the amino acid sequence of said DNA-binding domain of said protein exhibits at least 90%, 95%, 97%, and 98% homology with the amino acid sequence of SEQ ID NO:3 and the amino acid sequence of said ligand binding domain of said protein exhibits at least 75%, 80%, or 90% homology with the amino acid sequence of SEQ ID NO:4. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

New claims 20-26 encompass an isolated DNA encoding a variant protein having a DNA binding domain and a ligand binding domain without a functional limitation. However, the specification fails to teach how to make and use the whole genus of an isolated DNA encoding a variant protein having an N-terminal domain, a DNA binding domain, and a ligand binding domain without a functional limitation. The specification discloses an example of a specific species of human estrogen receptor and its splice variant but does not teach the whole genus of claimed products. It would require undue experimentation to test the function of a variant receptor which has essentially unlimited substitutions because the percent homology with SEQ ID NO: 3 and 4 are not defined and includes gaps and nonconserved substitutions and which includes variant proteins with only the N-terminal domain, a DNA binding domain, and the ligand binding domain. One skilled in the art cannot substitute amino acid randomly and predictably get functional protein (Bowie et al., Science, 1990). For example the receptor variants have other linkers or domains other than the N-terminal domain, a DNA binding domain, and the ligand binding domain which provide proper tertiary structural folding which is required for

proper ligand binding function and transcriptional activation. Furthermore, the claims encompass variant proteins with large deletions in a domain which is essential for function. Thus, the claims encompass a genus of large number of DNAs which encode non-functional receptors.

Amended claims 1-3, 6-8, 12, and 15-17 encompass new claims limitations drawn to the DNA binding domain targets the receptor protein to a selected hormone responsive element of a target gene and said ligand-binding domain recognizes and binds to an estrogen. However, the specification does not teach the genus of any selected hormone responsive element of any target gene and where the ligand binding domain binds an estrogen. The specification teaches the specific estrogen receptors of SEQ ID NO:5, 6, 21, or 25 with specific binding but does not teach variant receptors which targets any selected hormone responsive element of any target gene. The estrogen receptors are interact with specific response elements and for the transcription of specific transcripts. Claims 6-8 and 15-17 encompass a vector or cell comprising the DNA of claims 1-3. The vector of claim 6 and the host cell transfected with the vector of claim 6 comprise the DNA of claim 1 and thus encompass the same genus of large number of DNAs which encode receptors which cannot function as claimed.

Claims 7 and 8 encompass a cell transfected with DNA of claim 1 which is not in a vector. However, the specification

does not teach how to transfect cell with DNA which is not in a vector. One of skilled in the art do not transfect cells with cDNA which are not packaged in a vector because without the vector the expression copies of the DNA is not sufficient for expression of the protein product. Applicants argue that page 11 of the specification teaches the techniques for tranforming or transfecting host cells are quite known in the art reciting Sambrook et al. However, Sambrook et al do not transform or transfect cells without a vector.

6. Claims 1-3, 6-8, 15-17, and 20-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The reasons for the rejection has been set forth in the previous office action.

Applicants argue that amendment to claim 1 to recite an isolated DNA encoding an isolated human estrogen receptor protein provides adequate written description. However, the claims still encompass the DNA or vectors and cells comprising the DNA encoding a variant protein which is naturally occurring but not

disclosed in the specification to one of skilled in the art. Claimed DNA encoding protein variants encompass a large genus of nuclear receptors which are alleles or variants whose function has yet to be identified from different species of animal because the structure of the newly identified naturally occurring receptor is not known. *University of California v. Eli Lilly and Co. (CAFC) 43 USPQ2d 1398* held that a generic claim to human or mammalian when only the rat protein sequence was disclosed did not have written description in the specification.

Applicants argue that figure 4 shows the expression in tissues from several different species. However, the *University of California v. Eli Lilly* held that one skilled in the art cannot envision the specific sequence of the other species without a specific disclosure. Thus, any disclosure to a genus of homologs is not adequate written description.

Applicants argue that the skilled person can apply routine skill to isolate the corresponding complete cDNA without undue experimentation and with a reasonable expectation of success. However, the rejection is a lack of adequate description and not enablement. The reasonable expectation of success is directed to 35 USC 103 rejections and not 35 USC 112 written description rejection.

7. Claims 1-5, 7-8, and 10-11 are rejected under 35

U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is anew matter rejection.

The specification does not disclose the DNA with the claim limitation drawn to the function of "DNA binding domain targets the receptor protein to a selected hormone responsive element of a target gene and said ligand-binding domain recognizes and binds to an estrogen, thereby modulating expression of said target gene." Applicant did not point to the location in the specification which supports the new claim limitation.

The specification does not disclose the claim 22 limitation of "said DNA binding domain exhibits at least 97% homology with the amino acid sequence shown in SEQ ID NO:3." Applicant did not point to the location in the specification which supports the new claim limitation.

The specification does not disclose a generic invention of a DNA encoding an estrogen receptor without an N-terminal domain. Applicants state that the term estrogen receptor renders the term N-terminal domain redundant. While applicants appear to indicate that the term estrogen receptor encompasses an N-terminal domain, the claims 1-3, 6-7, 15-17, and 20-26 limitation is generic and

not disclosed in the specification.

Claim Rejections - 35 USC § 102

8. Claims 1-3, 6, 15-16 and 20-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Cabib et al.((C); U.S. 5,936,731).

The reasons for the rejection has been set forth in the previous office action.

Applicants argue that the term "isolated DNA" has the meaning commonly given to it in the molecular biology context which that the DNA is removed from its natural state to enable its examination in isolation. However, the claims encompass an isolated DNA in addition to other materials and the chromosome is removed from its natural state of inside the cell. The chromosomal DNA inherently comprises the sequences claimed. The claims are not limited to the species of DNA comprising specific SEQ ID NO: but encompasses a genus of DNA encoding a domain of the protein with percent identity to a SEQ ID NO:. Furthermore, Cabib et al. disclose the isolated human chromosome 14.

Claim Rejections - 35 USC § 103

9. Claims 1-3, 6-8, 15-17, and 20-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cabib et al.(C) in view

of Kausch et al.(A); U.S. '164).

Applicants traverse the rejection because of the arguments set forth above directed to Cabib et al. In the 35 USC 102 rejection. The answer for the argument has been set forth above as well.

10. Claim 12 is rejected under 35 U.S.C. 102(b) as being anticipated by Evans et al.((B); U.S. '233).

The reasons for the rejection has been set forth in the previous office action.

Applicants argue that the DNA binding domain has different percent identity between the claimed receptor and the Evan's receptor. However, the claims encompass variants because of the term "originates" which requires the starting point but not the end point. Furthermore, the N-terminal domain can be one amino acid.

11. No claims are allowed. Claims 4-5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS**

ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak, whose telephone number is (703) 305-7038. The examiner can normally be reached on Monday through Friday from 5:50 AM to 2:20 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Michael D. Pak

Michael Pak
Primary Patent Examiner
Art Unit 1646
21 July 2001